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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,805	10/03/2003	Madhavi Krishnan	UM-07718	3256
23535 7590 08/06/2007 MEDLEN & CARROLL, LLP 101 HOWARD STREET SUITE 350 SAN FRANCISCO, CA 94105			EXAMINER WILDER, CYNTHIA B	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/678,805

Applicant(s)

KRISHNAN ET AL.

Examiner

Cynthia B. Wilder, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 22 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 22-25 and 27-54 is/are pending in the application.
- 4a) Of the 'above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 22-25 and 27-54 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

1. Applicant's amendment filed 5/11/2007 is acknowledged and has been entered. Claims 1-22 have been canceled. Claims 22 and 30 have been amended. Claims 32-54 have been added. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

**This action is made FINAL.**

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Previous Rejections***

3. The prior art rejection under 35 USC 103(a) directed to claims 22, 25 and 27-31 as being unpatentable over Eck et al in view of Voribieff et al and further in view of Selvaganapathy is withdrawn in view of Applicant amendment and submission of a declaration under CFR 1.131 establishing reduction to practice prior to the date of the Selvaganapathy reference. The prior art rejection under 35 USC 103(a) directed to 22-25 and 27-31 as being unpatentable over Sogard in view of Tomishima et al is maintained and discussed below.

#### ***Declaration***

4. The declaration filed on 5/11/2007 under 37 CFR 1.131 is sufficient to establish reduction to practice prior to the Selvaganapathy et al reference. The cited support in the Selvagnapathy reference relies on the teachings of Krishnan et al (Science, vol. 298, pp 793-794). Applicant's declaration establishes

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reduction of practice prior to the teachings of the Selvagnapathy et al and prior to the teachings of Science reference by Krishnan et al.

***Claim Rejections - 35 USC § 103(a)***

5. Once again, claims 22-25 and 27-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sogard (2003/0077599, October 23, 2001) in view of Tomishima et al (5, 169,918, September 8, 1992). Regarding claim 22, Sogard teaches a method, comprising providing a reaction vessel comprising a top and a bottom, a heat source contacting said bottom of said reaction vessel, an active cooling means contacting said top of said reaction vessel, wherein said cooling means comprises a water bath and solution comprising a plurality of reactants; introducing said solution into said reaction vessel; and creating a convection cell by applying heat to said bottom of said vessel with said heat source and cooling said top of said vessel with said cooling means under such conditions that said reactants form a reaction product (Figure 1; Figure 3; 0013-0014; 0040-0045, 0047; and 0049-0052).

Sogard does not teach wherein the reaction vessel is configured with an aspect ratio of at least 3.3.

Tomishima et al teach an apparatus or reaction vessel comprising a top and bottom, a heat source contacting the bottom an active cooling means contacting the top, wherein the reaction vessel is configured with an aspect ratio of 4 or more (col. 5, lines 43-47; col. 6, lines 13-23, 60-68; col. 7, lines 20-25, 34-40). Tomishima et al teach that an apparatus configured with an aspect ratio of 4 or more with a temperature control system allows for a wide distribution of polymerization degrees and uniform temperature distribution (col. 6, line 61 to 68; col. 7, lines 18-25, 34-36).

It would have been obvious to one of ordinary skill in the art at the time of the claimed invention to have been motivated to modify the apparatus of Sogard to encompass an aspect ratio of at least 3.3 for the benefit of obtaining a uniform temperature distribution between the upward and downward directions of the reaction vessel as taught by Tomishima et al.

Regarding claim 23, Tomishima et al teach wherein a cross section of the reaction vessel may have elements that are rectangular or circular or elliptic or other similar forms (col. 7, lines 65-67).

Regarding claim 24, Sogard teaches the reaction vessel of claim 22, wherein the reaction vessel is with corners (see figure 1 and 2).

Regarding claims 25 and 27, Sogard teaches the method of claims 22 as previously described above. Sogard et al teach that the method and device can be used in hybridization and binding assays and may comprise amplified nucleic acids, via PCR techniques (0056-0057). Therefore, a nucleic acid comprising a target and primer substantially homologous to a least a portion of said target are inherent in the teaching of the nucleic acid amplification reaction via PCR.

Regarding claim 28, Sogard teaches the method of claim 22, wherein said reaction vessel comprises at least functionalized glass (0065, Figure 1).

Regarding claim 29, Sogard teaches the method of claim 22, wherein said reaction vessel is part of an array (0065, Figure 1).

Regarding claim 30, Sogard teaches the method of claim 22, wherein a temperature gradient of between about 5 degrees Celsius and 25 degrees Celsius or more preferably about 10 degrees Celsius/mm is used (0047).

Regarding claim 31, Sogard teaches the method of claim 22, also providing an input tube connected to a inlet port or fluidic interface port, which is in fluid communication with said reaction vessel (0053 and Figure 1).

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**Applicant's Traversal**

6. Applicant traverses the rejection on the following ground: Applicant states that Tomishima et al is directed towards plastics technology and not biological technology. Applicant states that Applicants submit that Tomishima et al is non-analogous. Applicant states that the Federal Circuit has outlined a basis definition for non-analogous art: (*Finish Engineering Co., Inc. v. Zerpa Industries, Inc.*, 806 F. 2d 1041, 1 USPQ2d 1114, 1116 (Fed. Cir. 1986). Applicant states that the Applicants have ordinary skill in biology they would not be motivated to consider references in plastics. Applicant states that Tomishima et al is not "within the field of inventor's endeavor". Applicant argues that Tomishima et al also is not "reasonably pertinent to the particular problem to which the invention was involved". Applicant states that this determination is made from the view point of one having ordinary skill in the art: A reference is reasonably pertinent if ....[it]...logically would have commended itself to an inventor's attention in considering his problem....IF it is directed to a different purpose, the inventor would accordingly have had less motivation or occasion to consider it. Applicant states that in addition, Tomishima et al and the Applicants' presently claimed embodiment do not solve the same problem. Applicant states that a person having ordinary skill in the art would not reasonably have expected to solve the Applicants' problem of moving reactants between a high temperature region and low temperature region within the same vessel by considering Tomishima et al that deals with maintaining reactants at a uniform temperature within the same vessel. Applicant states that even if the Examiner disagree that

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Tomishima et al is non-analogous art, the rejection still fails because there is no motivation for one having ordinary skill in the art to combine the teachings of Sogard and Tomishima et al. Applicant disagrees with the Examiner's rejection and states that because Sogard makes no mention of any desirability to modify an aspect ratio. Applicant states that in fact, Sogard makes no method of an aspect ratio whatsoever. Applicant states that the Examiner is reminded that suggestions and motivations to modify a reference must come from one having ordinary skill in the art, and not the Examiner. Applicant states that consequently, one having ordinary skill in the art, upon reading Sogard would not be motivated to seek Tomishima et al in order to consider modifying an aspect ratio. Applicant the Examiner is asked to take note of the recent Supreme Court opinion which says that a specific showing by the Examiner is required. Applicant states that Sogard teaches that Rayleigh-Benard convection cells may interfere with DNA hybridization and advocates the elimination of convection cells. Applicant states that Sogard, therefore, specifically teaches away from Tomishima's method and if anything suggests using reaction vessel with small h/d aspect ratios. Applicant further states that even if the Examiner decides that Sogard and Tomishima et al are properly combined the present rejection still fails because the combined references fail to teach all of the claimed elements. Applicant states that neither reference teaches "thermocycling of reactants: within a reaction vessel to form a reactant product. Applicant states that in fact, Tomishima et al explicitly states that their invention solves a problem related to non-uniform temperature distribution within a reaction vessel. Applicant states

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that clearly Tomishima et al teaches a reaction vessel having a single uniform temperature, not a reaction vessel having distinct temperatures areas (i.e., for example, a vessel capable of supporting thermocycling). Applicant states that nonetheless, without acquiescing to the Examiner's argument but to further the prosecution, and hereby expressly reserving the right to prosecute the original claims, Applicant have amended claim 22 to recite that the convection cell comprises "a temperature differential" thereby resulting in "thermocycling" of the reactants. Applicant states that theses amendments are made not to acquiesce to the Examiner's argument but only to further the Applicants' business interests, better define one embodiment and expedite the prosecution of this application.

***Examiner's Response***

7. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons that follow: In response to applicant's argument that Tomishima is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, the secondary reference of Tomishima is not cited for its use in i.e., plastics as argued by Applicant, but rather is cited for its teaching of an apparatus as required by the instant invention having as aspect ratio as described by Applicant's claims and instant specification. The apparatus of Tomishima et al comprises the same structural features as claimed in the instant

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invention and provides motivation for wanting an apparatus comprising an aspect ratio as claimed in the instant invention (see rejection above). Thus, the Examiner maintains that the reference of Tomishima is not non-analogous.

In regards to Applicant's arguments that the reference teaches away from the instant invention due the reference being non-analogous, MPEP 2143.01 states that the courts have established that "the prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed...." *Id.* In this case, the secondary reference of Tomishima does not criticize, discredit or discourage the solution claimed; rather Tomishima provides motivation for selecting an apparatus comprising a temperature control system and aspect ratio of about 3.3 or more. This argument is not persuasive.

In regards to Applicant's argument that there is no motivation to combine the teachings of Sogard with Tomishima et al, because Sogard makes no mention of any desirability to modify an aspect ratio, it is noted that KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 2007) (citing *KSR*, 82 USPQ2d at 1396).

In regards to Applicant's arguments that the reference of Sogard teaches away from the Tomishima's method because it suggest using reaction vessels with small h/d aspect ratios, it is noted that accordingly to Applicant's arguments

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an aspect ratio of about 3.3 (as claimed) or 4 (as taught by Tomishima) is not large but narrow and long (see page 8 of applicant's arguments). Likewise, MPEP 2123 states "disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or non-preferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "[A] known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994)".

In regards to Applicant's arguments that Sogard and Tomishima et al fails to teach all claimed elements because the references do not teach "thermocycling of reactants" within a reaction vessel", it is noted that a teaching of "thermocycling of reactants" as currently claimed is inherent in the teachings of Sogard, wherein amplification of DNA samples or cDNA occurs via PCR (0056). It is well known in the art that steps of PCR (polymerase chain reaction) requires "thermocycling of reactants" to produce amplification products.

In regards to Applicant's arguments that Tomishima et al teaches a reaction vessel having a single uniform temperature, not a reaction vessel having distinct temperature areas, it is noted that Tomishima was not cited for a vessel having distinct temperature areas, as this teaching is found in the primary reference of Sogard (0014). Nonetheless, contrary to Applicant's arguments Tomishima does teach a "conventional process" wherein fluid is transfer between distinct temperature areas. Tomishima teaches the follow:

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"[I]n the conventional processes in which all the monomer to be used is introduced into the polymerization apparatus at a time or in which polymerization is conducted while part of the monomer is being fed from an upper part of the polymerization apparatus, the monomer, which has a small specific gravity, is apt to be present more densely in the upper part of the polymerization apparatus because of the mild agitation, so that the monomer is not in a uniformly dispersed state in the lower part of the apparatus. In most cases, the monomer is present normally as a separated monomer phase layer on the latex phase. During polymerization, unreacted monomer evaporates from the separated layer of unreacted monomer phase in the upper part of the polymerization apparatus, is condensed by the condenser, and then returns to the monomer phase layer. Therefore, only the upper part of the polymerization apparatus is cooled, and removal of polymerization heat is not effective."

Applicant's claims are not sufficient to overcome the prior art rejections noted above. Accordingly, these rejections are maintained.

***New Ground(s) of Rejections***

***THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY APPLICANT'S AMENDMENT OF THE CLAIMS:***

***Claim Objections***

8. Claim 8, 35 and 42 are objected to because use of the trademark "plexiglas" has been noted in this application. It should be *capitalized* wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

***Claim Rejections - 35 USC § 102***

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 47-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Benett et al (US 2002/0127152, September 2002). Regarding claim 47, Benett et al teach a method comprising: providing a reaction vessel comprising a top and a bottom; a heat source contacting said bottom of said reaction vessel and a solution comprising a plurality of reactants and introducing said solution into said vessel and creating at least one convention cell comprising a temperature differential by applying heat to said bottom of said vessel with a heat source under conditions such that said reactants are thermocycled, thereby forming a reactant product (see 0021-0026, 00032-0034, 0036-0040 and 0048-0049).

Regarding claims 48 and 49, Benett et al teach thermocycling a sample via a PCR device to produce an amplified product (see 0021, 026 and 0034). Therefore, Benett et al inherently teaches a nucleic acid comprising a target and primers for amplifying the target.

Regarding claim 50, Benett et al teach wherein said reaction vessel comprises material selected from the group consisting of glass, silicones and metal(0023). Therefore, Benett et al meet the limitations of the claims recited

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above.

***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 32-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sogard (2003/0077599, October 23, 2001) in view of Tomishima et al (5,169,918, September 8, 1992). Regarding claims 32, 39, 40, 41, 47, 48 and 49, Sogard teaches a method, comprising providing a reaction vessel comprising a top and a bottom, a heat source contacting said bottom of said reaction vessel, an active cooling means contacting said top of said reaction vessel, wherein said

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cooling means comprises a water bath and solution comprising a plurality of reactants; introducing said solution into said reaction vessel; and creating a convection cell by applying heat to said bottom of said vessel with said heat source and cooling said top of said vessel with said cooling means under such conditions that said reactants form a reaction product (Figure 1; Figure 3; 0013-0014; 0040-0045, 0047; and 0049-0052). Sogard et al teach that the method and device can be used in hybridization and binding assays and may comprise amplified nucleic acids, via PCR techniques (0056-0057). Therefore, a nucleic acid comprising a target and primer substantially homologous to a least a portion of said target and thermocycling processes are inherent in the teaching of the nucleic acid amplification reaction via PCR.

Sogard does not teach wherein the reaction vessel is configured with an aspect ratio of at least 3.3.

Tomishima et al teach an apparatus or reaction vessel comprising a top and bottom, a heat source contacting the bottom and active cooling means contacting the top, wherein the reaction vessel is configured with an aspect ratio of 4 or more (col. 5, lines 43-47; col. 6, lines 13-23, 60-68; col. 7, lines 20-25, 34-40). Tomishima et al teach that an apparatus configured with an aspect ratio of 4 or more with a temperature control system allows for a wide distribution of polymerization degrees and uniform temperature distribution (col. 6, line 61 to 68; col. 7, lines 18-25, 34-36).

It would have been obvious to one of ordinary skill in the art at the time of the claimed invention to have been motivated to modify the apparatus of Sogard

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to encompass an aspect ratio of at least 3.3 for the benefit of obtaining a uniform temperature distribution between the upward and downward directions of the reaction vessel as taught by Tomishima et al.

Regarding claim 35, 42, and 50, Tomishima et al teach wherein a cross section of the reaction vessel may have elements that are rectangular or circular or elliptic or other similar forms (col. 7, lines 65-67).

Regarding claim 36, 43 and 51, Sogard teaches wherein said reaction vessel is part of an array (0065, Figure 1).

Regarding claim 37, 44-45 and 52-53, Sogard teaches wherein a temperature gradient of between about 5 degrees Celsius and 25 degrees Celsius or more preferably about 10 degrees Celsius/mm is used (0047).

Regarding claims 38, 46 and 54, Sogard teaches also providing an input tube connected to an inlet port or fluidic interface port, which is in fluid communication with said reaction vessel (0053 and Figure 1).

### ***Conclusion***

13. No claims are allowed. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be

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calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
JEFFREY FREDMAN  
PRIMARY EXAMINER

8/3/02